For Research Use Only

Pacritinib

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Catalog Number: CM04903

产品信息

Catalog Number:
CM04903

CAS号:
937272-79-2

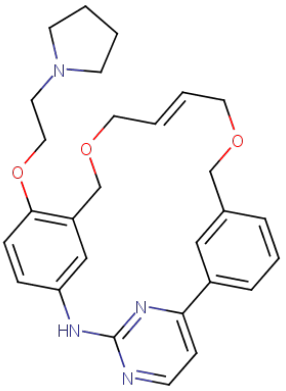
分子式:
$C_{28}H_{32}N_4O_3$

主要靶点:
FLT|JAK|Tyrosine Kinases

主要通路:
蛋白酪氨酸激酶|表观遗传|JAK/STAT信号通路|干细胞|血管生成

分子量:
472.58

溶解度:
H2O:<1 mg/mL,DMSO:11 mg/mL (23.27 mM),warmed,Ethanol:<1 mg/mL



靶点活性

JAK3:520 nM

体外活性

Pacritinib is an effective inhibitor of both wild-type JAK2 and JAK2V617F mutant (IC50: 19 nM). The IC50s of Pacritinib are 50 nM for TYK2, 520 nM for JAK3 and 1280 nM for JAK1. Pacritinib effectively permeates cells to modulate signaling pathways downstream of JAK2, whether agonist activated or mutationally activated. Pacritinib induces apoptosis, cell cycle arrest and antiproliferative effects in JAK2WT- and JAK2V617F-dependent cells. Pacritinib inhibits cell proliferation of Karpas 1106P (IC50: 348 nM) and Ba/F3-JAK2V617F (IC50: 160 nM), respectively. Pacritinib inhibits endogenous colony growth derived from erythroid (IC50: 63 nM) and myeloid progenitors(IC50: 53 nM), respectively.[1] SB1518 also inhibits FLT3 and its mutant FLT3-D835Y (IC50: 6 nM). Pacritinib inhibits FLT3 phosphorylation and downstream STAT, MAPK and PI3K signaling in FLT3-internal-tandem duplication (ITD), FLT3-wt cells and primary AML blast cells. Pacritinib treatment leads to a dose-dependent decrease of pFLT3, pSTAT5, pERK1/2 and pAkt in FLT3-ITD harboring MV4-11 cells with IC50 of 80, 40, 33 and 29 nM , respectively. Treatment of the primary AML blast cells with Pacritinib for 3 h leads to a dose-dependent decrease of pFLT3, pSTAT3 and pSTAT5 with an IC50 below 0.5 μM. Pacritinib induces apoptosis, cell cycle arrest and anti-proliferative effects in FLT3-mutant and FLT3-wt cells. Pacritinib inhibits cell proliferation of FLT3-ITD-harboring cells MV4-11 (IC50: 47 nM) and primary AML blast (IC50: 0.19-1.3 nM) cells.

体内活性

In JAK2V617F-dependent xenograft model, Pacritinib (150 mg/kg, p.o., q.d.) markedly ameliorates splenomegaly and hepatomegaly symptoms, with 60% normalization of spleen weight and 92% normalization of liver weight and is well tolerated without significant weight loss or any hematological toxicities, including thrombocytopenia and anemia. In JAK2V617F-dependent SET-2 xenograft model, Pacritinib dose-dependent inhibits tumor growth (40% for 75 mg/kg and 61% for 150 mg/kg).[1] Pacritinib treated once daily for 21 consecutive days, induces dose-dependent inhibition of tumor growth (38% for 25 mg/kg, 92% for 50 mg/kg and 121% for 100 mg/kg). Complete regression is observed in 3/10 and 8/8 mice for the 50 and 100 mg/kg/day groups, respectively.

细胞实验

Cells are seeded at 30-50% confluency in 96-well plates and are treated with different concentrations of compounds (in triplicate) for 48 h. Cell viability is monitored using the CellTiter-Glo assay.(Only for Reference)

描述

Pacritinib (SB1518) is an effective and specific inhibitor of JAK2 and FLT3 (IC50: 23/22 nM, in cell-free assays).

储存

Powder: -20°C for 3 years | In solvent: -80°C for 2 years

For technical support and original validation data for this product please contact
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